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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,396	12/21/2001	Danny Huylebroeck	2676-5174US	3530

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,396	HUYLEBROECK ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4 and 7-18* is/are pending in the application.

4a) Of the above claim(s) *7-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed December 16, 2004 is acknowledged and has been entered. Claims 5, 19, and 20 have been canceled. Claims 2 and 18 have been amended.

2. Claims 2-4 and 7-18 are pending in the application. Claims 7-17 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed November 10, 2003.

3. Claims 2-4 and 18 are currently under prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Grounds of Objection and Rejection Withdrawn

5. Unless specifically reiterated below, Applicant's amendment filed December 16, 2004 has obviated the grounds of objection and rejection set forth in the previous Office action mailed September 16, 2004.

Priority

6. Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in Europe on June 25, 1999. However, it is again noted that Applicant has not filed a certified copy of the EPO 99202068.5 application as required by 35 U.S.C. 119(b).

Grounds of Rejection Maintained and Response to Amendment and Arguments

Claim Rejections - 35 USC § 102

7. The rejection of claims 2-4 and 18 under 35 U.S.C. 102(b) as being anticipated by Sekido et al. (*Genes to Cells.* 1997; **2**: 771-783) (of record) is maintained.

This ground of rejection is set forth in section 17 of the previous Office action mailed September 16, 2004.

At pages 8 and 9 of the amendment filed December 16, 2004, Applicant has traversed this ground of rejection.

Applicant's arguments traversing this ground of rejection have carefully considered but have not been found persuasive for the following reasons:

Claims 2 and 18 are drawn to a process for identifying transcription factors, said process comprising providing cells with a nucleic acid sequence comprising two copies of the sequence "CACCT" separated by any number of nucleotides as bait and performing "a specificity test" to identify transcription factors that bind said nucleic acid sequence at both copies of said "CACCT" sequence. Claim 3 recites the transcription factors comprise separated clusters of zinc fingers. Claim 4 recites that said nucleic acid sequence originates from a promoter region.

Although the specification does not expressly define "a specificity test", the disclosure at pages 39 and 40 (paragraph [0103]), for example, implies the test can include an analysis and comparison of the DNA binding specificities of a transcription factor and mutational variants thereof, or alternatively an analysis and comparison of the DNA binding specificities of a transcription factor for an element of a promoter, and mutational variants thereof, to which the transcription factor normally binds, as measured indirectly using a reporter gene construct, such as that described.

Sekido et al. teaches that which is set forth in section 17 of the previous Office action, beginning at page 9.

Applicant has argued that the prior art does not teach the provision of a cell comprising a nucleic acid sequence comprising a first "CACCT" sequence separated from a second "CACCT" sequence by a spacer sequence of less than 400 base pairs. Sekido et al. teaches providing a cell having multiple copies of a nucleotide sequence of

a promoter region of a gene encoding a lens cell protein; see entire document (particularly page 775, Figure 3 and its legend, and page 781, column 2). The promoter region, which is designated "HN", comprises the sequence "CACCT", which is flanked on either end by additional sequences; see, e.g., page 775, Figure 3. Sekido et al. discloses that an octameric form of the HN fragment was inserted upstream of the promoter of pδ51LucII and cloned into chicken embryo lens cells (page 781, column 2). Therefore, the cell provided by Sekido et al. comprises a nucleic acid molecule comprising eight tandem direct repeats of the HN fragment comprising of the sequence, or a nucleic acid sequence comprising "CACCT-N-CACCT", where "N" is a finite number of nucleotides (i.e., 55 base pairs) separating each copy of the sequence "CACCT". Sekido et al. teaches the disclosed process identifies the transcription factor δEF1 as binding to the sequence "CACCT"; see, e.g., page 775, Figure 3.

For further clarity, it is noted that the octameric form of the HN fragment inserted into the plasmid transfected into the cells provided by Sekido et al. is depicted by Funahashi et al. (*Nucleic Acids Res.* 1991; **19** (13): 3543-3547) and Kamachi et al. (*Mol. Cell. Biol.* 1993 Sep; **13** (9): 5206-5215), which are cited by Sekido et al. at page 781 in column 2, as disclosing the octameric form. Funahashi et al. depicts the construct in Figure 1 at page 3544 and describes its construction at, e.g., page 3543, column 2. Kamachi et al. depicts the construct in Figure 1 at page 5207 and discloses the octamerization process at page 5207 beginning in column 1.

In addition, Applicant has argued that the prior art does not teach screening a library encoding potential transcription factors. Claim 18 recites only two active steps: (a) providing a cell and (b) performing a specificity test. The objective of the claim, namely identifying transcription factors is met by the second active step alone, since the claim recites, "performing a specificity test to identify said transcription factors". Sekido et al. teaches the provision of a cell comprising a first "CACCT" sequence separated from a second "CACCT" sequence by a spacer sequence of less than 400 base pairs. In addition, Sekido et al. teaches the disclosed process identifies the transcription factor δEF1 as binding to the sequence "CACCT"; see, e.g., page 775, Figure 3. Sekido et al.

teaches the transcription factor δEF1 comprises separated clusters of zinc fingers; see, e.g., the abstract. Because Sekido et al. teaches that the transcription factor δEF1 represses the transcription of a reporter gene to which the nucleic acid molecule comprising multiple copies of the promoter region comprising the sequence "CACCT" is operably adjoined, Sekido et al. demonstrates that δEF1 binds specifically to the sequence to regulate its activity in the cell; see, e.g., page 775, Figure 3. Sekido et al. teaches testing the DNA binding specificity of δEF1 using a naturally occurring promoter region and mutational variants thereof, or alternatively using the naturally occurring transcription factor and mutational variants thereof, to define the characteristics of the interactions between the protein and the polynucleotide sequence to which it binds; see, e.g., page 775, Figure 3.

Claim Rejections - 35 USC § 103

8. The rejection of claims 2-4 and 18 under 35 U.S.C. 103(a) as being unpatentable over Mak et al, (*DNA Cell Biol.* 1996; **15**: 1-8) (of record) in view of Sekido et al. (*Genes Cells.* 1997; **2**: 771-783) (of record) is maintained.

This ground of rejection is set forth in section 17 of the previous Office action mailed September 16, 2004.

At pages 9-11 of the amendment filed December 16, 2004, Applicant has traversed this ground of rejection.

Applicant's arguments traversing this ground of rejection have carefully considered but have not been found persuasive for the following reasons:

Applicant has argued that the combination of references would produce a process that screens a cDNA library for transcription factors with single DNA-binding domains that bind to a single E-box site. Although the Examiner disagrees with Applicant's assertion that the combination of references would not suggest the claimed process, it is duly noted that a single DNA-binding domain interacts with a single E-box site (i.e., a single zinc finger interacts with a single "CACCT" sequence).

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as explained in the previous Office action, it would have been obvious to one ordinarily skilled in the art at the time of invention to practice the method of Mak et al. using the promoter region disclosed by Sekido et al. comprising a polynucleotide sequence comprising multiple copies of the sequence "CACCT" separated by a spacer sequence of a finite number of nucleotides, which is less than 400, as bait to screen a cDNA library to identify novel transcription factors that bind the promoter region's polynucleotide sequence because Mak et al. teaches a process that can be used to screen a cDNA library to identify and isolate cDNA molecules encoding novel transcription factors comprising providing a cell comprising a reporter gene construct containing an operably adjoined promoter region comprising multiple copies of an E box, which is used to as bait in the process, and Sekido et al. teaches a promoter region comprising a polynucleotide sequence comprising multiple E-box sites having the sequence "CACCT" to which transcription factors, including activators and repressors, such as δEF1 comprising separated clusters of zinc fingers, bind, which can be used to identify such transcription factors. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to identify and isolate cDNA molecules encoding novel transcription factors,

which bind to the polynucleotide sequence disclosed by Sekido et al. to regulate the transcription of the gene encoding δ1-crystallin.

In response to Applicant's other arguments, the limitations of the claims are met by the combination of the references.

Conclusion

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
March 17, 2005

LARRY R. HELMS, PH.D
PRIMARY EXAMINER